REMARKS

Rejection under UCS 35, 112, first paragraph

The Examiner has rejected Claims 85 and 86 as containing subject matter that is not described in the specification in such a way as to enable one skilled in the art to which it pertains. In particular, the Examiner states:

> On page 26, lines 7 – 11 [of the pending specification], it is taught that "[t]he ability of purified 5A11 monoclonal anti-Aβ antibody to bind ^{125}I- $A\beta_{1-40}$ was unaffected by the presence of human serum albumin (HAS) [sic] at 60 mg/ml, even though this was a 500--fold molar excess over the antibody concentration (Table 3)." The instant claims are not limited as to what beta-amyloid protein is used or what the antibody is. Since the specification teaches that this particular antibody and antigen is used with HAS, the claims should so limited [sic].

The Applicant respectfully disagrees.

A. The Examiner had Failed to Establish the Required *Prima Facie* Showing of Lack of Enablement

It is well established that an application as filed *must* be taken as being enabled for a claimed invention unless an Examiner establishes otherwise. *See* MPEP 2164.04, *citing In re Marzocchi, 169 U.S.P.Q. 367* (CCPA 1971); *see also In re Brana, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). The initial burden is on the Examiner* to present *evidence or fact-based reasons* why a person skilled in the art would not be able to *make and use* the claimed invention without undue experimentation. *See*, MPEP 2164.04.

An Examiner must carry this burden with findings of fact and/or factors and reasoning sufficient to support an allegation of inadequate enablement. *See*, MPEP 2164.04. In is well established that a general allegation of non-enablement based only on the opinion of an Examiner is *not a sufficient reason* to make or support an enablement rejection. *See*, MPEP 2164.04, *citing In re Marzocchi, Id; In re Wright*, 27 U.S.P.Q. 2d (Fed. Cir. 1993).

In the present case, the Examiner has failed to provide *any* evidence or facts (much less a preponderance) support why one of ordinary skill in the mature and developed art of antibody-antigen immune complex formation would not be able to make and use the claimed method without undue experimentation. No express findings of fact have been presented. No *evidence* or *supportable reasoning* has been produced to support the cursory allegation that the claimed invention is not enabled. Indeed, the required *prima facie* showing is not possible

based on the mature state of the art, the detailed teachings of the specification and the evidence of record in this case lineage.

Accordingly, the Examiner has erred by failing to establish the required *prima facie* showing of lack of enablement. The new rejection of Claims 85 and 86 is therefore improper and should be withdrawn.

B. The Examiner has misapplied a Working Examples Requirement that Does *not* Exist under U.S. Patent Law or Rules

It is firmly and clearly established under U.S. patent law that the presence of absence of working examples, or any particular number of working examples, is not the test of whether a claimed invention is adequately enabled. *See*, MPEP 2164.02.[1] Rather, what the patent law requires is determining whether a skilled artisan can make and use the invention as claimed without undue experimentation, based on both the teachings of the specification and the general knowledge in the relevant art. This determination is fact-based and must consider a variety of factors, as the Federal Circuit Court of Appeals made clear in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1998); *see also*, MPEP 2164.01(a). These Wands factors (as they are widely known) include:

(1) The quality of experimentation required given the content of the specification;

(2) The amount of direction/guidance provided in the specification;

(3)The presence or absence of working examples;

(4) The nature of the invention;

(5) The state of the prior art;

(6) The relative skill of those in the art;

(7) The level of predictability in the art; and

(8) The breadth of the claims.

Among these factors, the amount of guidance provided in the specification and the level of skill and knowledge in the relevant art are particularly important. *See*, MPEP 2163.03, *citing In re Fisher*, 166 U.S.P.Q. 18 (CCPA 1970). Again, the ultimate test is considering the various Wands factors remains clear:

> "As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of

[1] In fact, no working examples are required at all as long as the skilled artisan can practice the claimed invention without an undue amount of experimentation. *See*, MPEP 2164.02.

the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." MPEP 2164.01(b), *citing In re Fisher, Id.*

In the present case, the Examiner has nonetheless misapplied a number of working examples the to the Applicant's specification and claimed invention and has improperly based the new enablement rejection on nothing more that the absence of actual working examples *for each preferred species* of antibody-antigen immune complex formation recited in the claims. The Examiner has failed to consider the Wands factors, has provided *no other basis* for why the application, as filed, would not enable the skilled artisan to *make and use* the claimed invention without undue experimentation. This error is all the more striking considering that the specification does, in fact, contain detailed working examples teaching the antibody-antigen immune complex formation of the claimed method.

Accordingly, the Examiner has erred by failing to apply the proper enablement analysis and misapplying an improper presence/absence of particular working examples test to support an assertion of inadequate enablement. The new rejection of claims 85 and 86 is therefore, improper and should be withdrawn.

C. Consideration of the *Wands* Factors Irrefutably Leads to a Conclusion that the Claimed Invention is Sufficiently Enabled.

To satisfy the enablement requirement, a specification must teach one of skill in the art to which the invention pertains to make and use the claimed invention without undue experimentation. As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied. MPEP 2164.01(b), *citing In re Fisher, Id.*

The enablement analysis *must* be conducted from the viewpoint of persons skilled in the field of the invention at the time the patent application was filed. *See Ajinomoto Co., Inc. v. Archer-Daniels-Midland Co.,* 56 U.S.P.Q. 2d 1385 (Fed. Cir. 2000). By law, an Examiner is not considered one skilled in the art. "The examiner should **never** make the determination based on personal opinion. The determination should always be based on the weight of all the evidence." MPEP 2164.05.

The determination is fact-based and must consider a variety of factors, generally known as Wands actors. These factors are discussed at length below.

1. The Nature of the Invention and the Breadth of the Claims

The invention as claimed is directed towards a method for forming an immune complex between an antibody with specificity towards beta-amyloid and its antigen in the presence of physiological levels of human serum albumin.

In order to make and use the invention as most broadly claimed (Claim 1), a skilled artisan need only be able to incubate an antibody with specificity towards a beta-amyloid epitope in the presence of physiological levels of human serum albumin. This is not beyond the ken of those practiced in the art. As discussed in the next section, the artisan of skill in the mature and well-developed art of antibody use can *readily* practice these steps without undue experimentation.

2. The mature State of the Art and its High level of Skill

The Federal Circuit Court of Appeals, the USPTO Board of Appeals and the USPTO itself have all recognized that the production and use of antibodies (including various immunoaffinity techniques) is a mature field with a very high level of skill. For example, in its Revised Interim Written Description Guidelines (hhtp://www.uspto/gov/web/_patents/_guides.htm), the USPTO discusses exemplary antibody claims and technology and clearly states:

> "This is a mature technology where the level of skill is high and advanced ... antibody technology is well developed and mature..." *See*, Written Description Guidelines at p. 59-60.

The Federal Circuit, in favorably commenting on the USPTO's Guidelines, acknowledged the mature nature of the antibody art and its high level of skill and knowledge in *Enzo Biochem. Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316 (Fed. Cir. 2002). Other Federal Circuit decisions have also recognized the mature nature of antibody production, characterization and use and the high level of skill in this art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986). The USPTO Board of Patent Appeals too has explicitly recognized the mature state of this art. *See, e.g., Ex Parte D.* 27 USPQ2d 1067 (BPAI 1993).

Beyond this evidence, "Patents and printed publications in the art should be relied upon to determine whether an art is mature and what the level of knowledge and skill is in the art." *See, In re Haynes Microcomputer products, Inc. Patent Litigation*, 982 F.2d at 1527 (Fed. Cir. 1992). In regards to the present case, the scientific literature and several well-known and standard references in this art also clearly evidence the advanced state of antibody production, characterization and use, and the high level of knowledge and skill in this art. For example, an

entire seven hundred pare manual, Antibodies: A Laboratory Manual, Harlow and Lane (1988), Cold Spring Harbor Laboratory, is devoted solely to the production, characterization and use (including immunoaffinity techniques and immune complex formation) including six detailed chapters on the use of antibodies. Another widely-known and standard reference in this art is Current Protocols in Molecular Biology, Volume 2, John Wiley & Sons (1992), which devoted over 102 pages in Section 11 solely to the production, characterization and use of antibodies, including the immunoaffinity techniques and the formation of immune complexes. This manual is used by those skilled in this art and its techniques are considered standard. Both of these detailed technical references underscore the advanced nature of this mature art and the high level of skill and knowledge in antibodies, their features and use.

3. The Detailed Guidance & Working Examples Provided in the Specification

Against this backdrop of extensive knowledge and skill in this mature art, the Applicant file a 61-page very detailed specification describing the invention, as presently claimed.

4. The Quantity of Experimentation Required Given the Detail of the Specification

Given the nature of the invention, the mature nature of the art to which the invention relates, the very high level of knowledge of those skilled in this art and the detailed guidance and working examples provided by the Applicant in the specification, there is little experimentation (much less undue experimentation) required for the skilled artisan to make and use the invention as claimed. All such an artisan need do to make and use the claimed invention is follow the teachings of the specification and employ their knowledge of well-known art techniques such as antibody use and immunoaffinity techniques to carry out the required steps of the claimed method (as most broadly set out in Claim 85).

The Examiner is reminded that the quantity of experimentation is not the determining factor if the experimentation is regularly performed in the art. For example, the Federal Circuit determined that experimentation requiring $50,000 and 6-12 months of time per experiment was not unreasonable since the method to determine dose response was set forth in the specification. *See,* MPEP 2165.06(I), *citing United States v. Telectronics, Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988). Additionally, in *In re Wands*, the court clearly determined that quantity of experimentation was not undue if it merely consisted of routine screening or methods routine in biotechnology, as is the case with the present claimed invention. *See, In re Wands* a, 858 F.2d 731 (Fed. Cir. 1988).

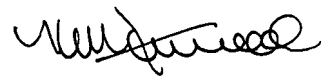
In conclusion, conducting the required enablement assessment by considering the *Wands* factors, consulting the publications of record establishing the state of the art in this field, and reading the detailed 61-page specification through the eyes of a skilled artisan inevitably leads to the following conclusion: One of ordinary skill in the art would readily be able to make and use, *without undue experimentation*, the presently claimed method for the formation of an immune complex between anti-beta-amyloid antibodies and their antigen in the presence of physiological levels of human serum albumin. The specification therefore satisfies the enablement requirement.

Accordingly, Applicant submits that the outstanding enablement rejection of Claims 85 and 86 are improper and unsustainable and should be withdrawn.

Summary

In light of the above Response, the passing of the subject patent application to allowance is respectfully requested.

Respectfully submitted,



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